

Claims

1. A method for determining whether a compound is a potentially useful dopamine β -hydroxylase inhibitor by

5 a. contacting said compound with a dopamine β -hydroxylase polypeptide region that comprises an amino acid corresponding to amino acid position 87, amino acid position 100, or amino acid position 331 of SEQ ID NO:35; and

b. detecting binding of said compound to said region, wherein binding indicates that said compound is potentially an inhibitor of dopamine β -hydroxylase.

10 2. The method of claim 1, wherein said amino acid corresponding to amino acid position 87 is methionine, valine, isoleucine, or leucine.

15 3. The method of claim 1, wherein said amino acid corresponding to amino acid position 100 is glutamic acid, aspartic acid, asparagine, or glutamine.

4. The method of claim 1, wherein said amino acid corresponding to amino acid position 331 is aspartic acid, glutamic acid, asparagine, or glutamine.

20 5. The method of claim 1, wherein said region comprises 5-20 amino acids on either side of an amino acid corresponding to amino acid position 87, 100, or 331 of SEQ ID NO: 35.

25 6. A method for determining whether a compound is a potentially useful dopamine β -hydroxylase inhibitor by

a. contacting said compound with a dopamine β -hydroxylase polypeptide region that comprises an amino acid corresponding to amino acid position 87, amino acid position 100, or amino acid position 331 of SEQ ID NO:35; and

30 b. detecting dopamine β -hydroxylase biological activity, wherein binding indicates that said compound is potentially an inhibitor of dopamine β -hydroxylase.

7. The method of claim 6, wherein said amino acid corresponding to amino acid position 87 is methionine, valine, isoleucine, or leucine.

5 8. The method of claim 6, wherein said amino acid corresponding to amino acid position 100 is glutamic acid, aspartic acid, asparagine, or glutamine.

9. The method of claim 6, wherein said amino acid corresponding to amino acid position 331 is aspartic acid, glutamic acid, asparagine, or glutamine.

10 10. The method of claim 6, wherein said region comprises 5-20 amino acids on either side of an amino acid corresponding to amino acid position 87, 100, or 331.

15 11. The method of claim 6, wherein said DBH biological activity is norepinephrine biosynthesis.

12. The method of claim 1, wherein said candidate compound is useful for the treatment of a patient with congestive heart failure, or chronic activation of sympathetic nerve function.

20 13. The method of claim 6, wherein said candidate compound is useful for the treatment of a patient with congestive heart failure, or chronic activation of sympathetic nerve function.

25 14. The method of claim 1, wherein said inhibitor increases dopamine levels.

15. The method of claim 6, wherein said inhibitor increases dopamine levels.

16. The method of claim 14, wherein said increase in dopamine levels benefits renal function in a patient with congestive heart failure.

17. The method of claim 15, wherein said increase in dopamine levels benefits renal function in a patient with congestive heart failure.

18. An isolated polypeptide region comprising the sequence of SEQ ID NO:38, 42, or 46.

19. A method for determining whether a patient has an increased risk of miscarriage, still birth, or fetal or neonatal death, said method comprising determining whether a dopamine β -hydroxylase polynucleotide sequence of said patient has a mutation at the consensus donor site between the first exon and first intron, or in a polynucleotide that encodes a region comprising either aspartic acid at amino acid position 100, aspartic acid at amino acid position 331, or valine at amino acid position 87, wherein a mutation indicates that said patient has an increased risk for having a miscarriage, still birth, or fetal or neonatal death.

20. A method for determining whether a patient has an increased risk of noradrenergic disease, depression, dementia, bipolar disorder, schizophrenia, or attention deficit/hyperactivity disorder, said method comprising determining whether a dopamine β -hydroxylase polynucleotide sequence of said patient has a mutation at the consensus donor site between the first exon and first intron, or in a polynucleotide that encodes a fragment comprising either aspartic acid at amino acid position 100, aspartic acid at amino acid position 331, or valine at amino acid position 87, wherein a mutation indicates that said patient has an increased risk for having noradrenergic disease, depression, dementia, bipolar disorder, schizophrenia, or attention deficit/hyperactivity disorder.